REMARKS

Claims 1-6 and 8-12 are pending. Claims 7 and 13-15 have been cancelled as being drawn to a nonelected invention. Claim 5 has also been cancelled. Claims 10 and 12 have been amended. The amendment to claim 10 is supported by disclosure at page 13, lines 26-27 of the specification. The amendment to claim 12 is supported by the claim as originally filed.

No new matter has been added by this amendment.

Restriction/Election

Applicant affirms the election of the invention of Group I, claims 1-6 and 8-12.

Specification

The specification was objected to because it contains an embedded hyperlink and/or other form of browser-executable code. As requested, Applicant has amended the specification to delete all embedded hyperlinks and/or other form of browser-executable. Therefore, Applicant requests that this objection be withdrawn.

35 U.S.C. § 101

Claims 1-6 and 8-12 were rejected for lack of utility on the grounds that the claimed invention is not supported by either a specific and/or a substantial utility or a well-established utility. The Examiner's position is that "the disclosed uses of the nucleic acids or encoded proteins are not specific and are generally applicable to any nucleic acid and/or proteins". *See* Office Action at page 3. Applicants traverse.

Only one specific, substantial, and credible utility is needed for a claim to meet the requirements of 35 U.S.C. § 101. On page 2, line 9, of the specification, Applicants disclose that OBP1, the claimed gene and gene product, "provides a marker for osteoblasts". At line 5-7 of the same page, Applicants disclose:

> As shown in Fig. 2, a 1 kB mRNA signal was detected very strongly in differentiated rat osteoblasts, but not in the other rat tissues assessed. These data demonstrate that OBP1 is selectively expressed in rat osteoblasts. This pattern of expression was previously observed with osteocalcin, a marker for osteoblast phenotype.

And on page 1, lines 9-10, of the specification, Applicants state "bone formation is promoted by stimulating the growth, differentiation, or activation of osteoblasts." Thus, the utility asserted by the specification is that the claimed composition is as a marker for osteoblasts, bone-forming cells.

The Revised Interim Utility Guidelines further provide guidance regarding the meaning of the terms "specific", "substantial" and "credible", and further states that the utility requirement may be fulfilled by a "well established utility". Applicants submit that the asserted utility meets the requirements of the Guidelines as discussed below.

With respect to "credible utility", the Guidelines states:

> An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion.

The Guidelines further states that a credible utility for a nucleic acid could be as a probe or marker. Here, Applicants have shown data that establishes that the claimed nucleic acid and corresponding protein is detected strongly in osteoblasts, but not in other tissues. Thus, the logic underlying the assertion is sound. Moreover, the facts (*i.e.*, the data in Fig. 2 showing the expression pattern of the gene in various tissues) are consistent with the logic underlying the

assertion. Applicants assert that the claimed nucleic acids and encoded proteins can be used, *inter alia*, as a marker for osteoblasts based on their expression profile. *See* Specification at page 2, lines 4-9. Thus, the asserted utility is credible.

Next, the Guidelines addresses "specific utility". The utility guidelines contrast a utility that is specific to the subject matter claimed with one that is generally applicable to the broad class of the invention. The Guidelines states:

> A utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target.

In the present case, Applicants have disclosed a target, osteoblasts. A marker for osteoblasts is a specific utility. This contrasts with a general utility that would be applicable to the broad class of the invention – for example, any bone cell. Rather the asserted utility is that the claimed composition is useful for a specific unique type of bone cell. Accordingly, the nucleic acids of the present invention have a specific utility as markers for identifying a particular subset of cells associated with bone, *i.e.*, osteoblasts.

With respect to "substantial utility" the Examiner stated at page 3, paragraph 8:

> . . . no substantial utility has been established for the claimed subject matter. For example, a nucleic acid could be used to detect a protein. The protein could then be used in conducting research to functionally characterize the protein, *e.g.* its possible role in bone formation. The need for such research clearly indicates that the protein and/or its function is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility.

Applicants traverse.

Applicants submit that the asserted utility meets the requirements of "substantial utility". According to the Guidelines, a substantial utility is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. In the present case, no further research is required to establish that the claimed compositions identify osteoblasts. As shown in Figure 2 of the specification, expression of OBP1 mRNA is restricted to osteoblasts (*i.e.*, ROB 30 cells), when compared to other cell and tissue types. Accordingly, expression of OBP1 has substantial utility for differentiating between osteoblasts and other cell and tissue types.

Moreover, the Guidelines contrast "substantial utility" with "throw away" utility with the following example.

> Note that "throw away" utilities do not meet the tests for a *specific* or *substantial* utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use).

In the present case, the utility is specific because it applies to one specific type of bone cell, *i.e.*, an osteoblast, rather than any cell or any bone cell for that matter. The utility is substantial, because few markers exist for identification of osteoblasts and identification/isolation of such cells are a "real world" goal in the field of medicine.

The utility requirement is also fulfilled if the claimed invention has a "well established utility". The Guidelines describes this category as

> A specific, substantial, credible utility which is well known, immediately apparent, or implied by the specification's disclosure for the properties of the material, alone or taken with the knowledge of those skilled in the art.

In the present case, it is "immediately apparent" from the specification that the compositions are useful to identify and isolate osteoblasts, because the expression profile of the gene is specific for

that type of cell and obtaining such cells is a well established medical goal. The utility is also implied by the data that shows tissue-specific expression of the gene. Furthermore, the specification states that the claimed composition has the same utility as osteocalcin (page 2, lines 6-8, of the specification), a well established marker of osteoblasts. Taken alone or together with the knowledge in the art of osteogenesis, the utility of the claimed composition as an identifier of osteoblasts is a "well established" utility.

Applicants submit that the specification more than meets the requirements of 35 U.S.C. §101. Therefore, Applicants request withdrawal of this rejection.

35 U.S.C. § 112, first paragraph

Claims 1-6 and 8-12 were rejected for lack of enablement because one skilled in the art would not know how to use the claimed invention since it lacks utility. Applicants have disclosed the sequence on which the newly claimed subject matter is based. Once the nucleic acid sequence and amino acid sequence is known, it is well within the skill of those in the art to make the nucleic acid or protein using recombinant or synthetic methods as described throughout the specification, *e.g.*, at page 11, line 1, to page 12, line 25, and at page 20, lines 1-21.

As is discussed above, the utility of the compositions as markers for osteoblasts has been established. Methods of using the compositions for this purpose are well known in the art and described in the specification, *e.g.*, Fig. 2 and page 35, lines 7-10, of the specification. Thus, the rejection of these claims for lack of enablement should be withdrawn.

35 U.S.C. § 112, second paragraph

Claims 5 and 10 were rejected for indefiniteness. According to the Examiner, claim 5 is vague and indefinite for reciting "which hybridizes under high stringency conditions", and claim 10 lacks the necessary active steps to carry out the method. Claim 5 has been cancelled. Claim 10 has been amended to include the active step of isolating the polypeptide. Therefore, claim 10 is clear and definite. Thus, Applicants request withdrawal of this rejection.

35 U.S.C. § 102

Claims 1-3, 5-6, and 8-12 were rejected under 35 U.S.C. § 102(b) as being anticipated by Bonaldo *et al.* (Genome Research (1996) 6:791-806; GenCore version search report). According to the Examiner, Bonaldo *et al.* teach normalization and subtraction approaches to facilitate gene discovery and disclose a nucleic acid comprising nucleotides 319-555 of SEQ ID NO:1 and its corresponding encoded amino acid sequence as SEQ ID NO:2. This rejection is traversed.

Position 389 of SEQ ID NO:1 is "g" nucleotide. In the sequence alignment using the Bonaldo sequence (Accession BF 550603; copy attached hereto, Appendix A), position 251 is "n". "n" represents any of the nucleotides or "another" or "unknown", *i.e.*, the identity of the nucleotide at that position is not disclosed at all. The Bonaldo reference discloses that the nucleotide at that position can be anything at all. The claims require that the nucleotide at position 389 of the claimed composition be a guanine nucleotide. Therefore, the Bonaldo reference does not anticipate the claimed invention, and this rejection should be withdrawn.

CONCLUSION

Applicant submits that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

The Commissioner is hereby authorized to charge any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311 (Reference No. 25669-016).

Respectfully submitted,

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APPENDIX A

☐ 1: BF550603. UI-R-C1-kq-d-07-0...[gi:11660333]

IDENTIFIERS

dbEST Id:	7080046
EST name:	UI-R-C1-kq-d-07-0-UI.r1
GenBank Acc:	BF550603
GenBank gi:	11660333

CLONE INFO

Clone Id:	UI-R-C1-kq-d-07-0-UI (5')
Source:	The University of Iowa Program for Rat Gene Discovery and Mapping (Val Sheffield, Bento Soares and Tom Casavant)
Id as DNA:	UI-R-C1-kq-d-07-0-UI
Id in host:	UI-R-C1-kq-d-07.r1
DNA type:	cDNA

PRIMERS

Sequencing:	M13 Forward
PolyA Tail:	Unknown

SEQUENCE

CACGAGGCACATGTGCATAGGAACATGCGGTTGTGCACACTTGTGCACAGATGCCTGGCG
TATTCATGCACCTATATAGGTGCCAACATCCCTAGCCTGCTTCCTCAGGGGGCCTTTAGG
ACCTGAGCCCTGTCATCATTTCAGACATGGGCCTTGGCCCTGAGCAGAGGCCAAGGAAGC
ATGAAGGTGCGTTCTAGGTCTTGTTTTCTCAGACCTGTTTTCCCGTTGGGGGAGGCAGGA
GGGGGCCGCANTAATACTCCATCAAGCCCATTCCAGAGAGGAGAGACACCCACCACACTC
AGAACCTCCCAAGTATGTGAGGACTTTCCTTATGGGAACCCTGAGGTTCCCTCAGTTATT
TCCTGCCTGAGAAGACAAGTCAGTCTTCCATCTCTGAGCCCAGGTCTCCTAGTCTGATAG
CTGGGGCAGCCTCTCCCATTTTGCATGTCTCTTTGGTGCAGCC

Entry Created:	Dec 12 2000
Last Updated:	Dec 12 2000

COMMENTS

cDNA Library Preparation: M.B. Soares Lab Clone distribution: clones will be available through Research Genetics (www.resgen.com) This clone is also available through the I.M.A.G.E. Consortium at LLNL (info@image.llnl.gov). IMAGE ID= 1775573

LIBRARY

Lib Name:	UI-R-C1
Organism:	Rattus norvegicus
Strain:	Sprague-Dawley
Develop. stage:	Adult
Lab host:	DH10B (Life Technologies)
Vector:	pT7T3D-Pac (Pharmacia) with a modified polylinker
R. Site 1:	Not I